REMARKS

Status of the claims

Claims 1-35 are pending in this application. Claims 8-17 and 23-35 are withdrawn from consideration. Claims 3 and 19 are canceled. As such, claims 1-2, 4-7, 18 and 20-22 are currently under consideration in this application.

Amendments to the claims

Claims 1, 2, 4-7, 18 and 20-22 have been modified to recite "an arrestin chimera" rather than "modified arrestin". This amendment clarifies the nature of the claimed protein and such arrestin chimeras are described throughout the specification, for example, see pages 20 and 52-60. As such, this amendment adds no new matter.

Claim 2 has been amended to recite that the ubiquitin moiety or fragment of ubiquitin is fused in frame to the arrestin. This amendment clarifies the relationship of the ubiquitin and the arrestin elements of the chimera recited in claim 1. This amendment is fully supported in the specification, see for example page 53, paragraph [0207]. As such, no new matter is added by this amendment.

Claim 5 has been amended to correct the antecedent basis of the terms "ubiquitin" and "arrestin" by reciting the full terms recited in claim 1 – i.e., "arrestin or fragment of arrestin" and "ubiquitin moiety or fragment of ubiquitin". As such, this amendment adds no new matter.

Claim 7 has been amended to correct an error in grammar and place an "or" between "SEQ ID NO: 4" and "SEQ ID NO: 6". As such, this amendment adds no new matter.

Claim 18 has been amended to clarify that the ubiquitin moiety of the arrestin chimera recited in claim 1 comprises one or ubiquitin chains. This amendment is fully supported in the specification, for example on page 21, paragraph [0086]. As such, this amendment adds no new matter.

Applicants respectfully request entry of the claims as amended.

Oath/Declaration

The Office Action states that the oath or declaration is defective because the inventors did not include a date of execution with the signature. Applicants thank the Examiner for identifying this error. Applicants are in the process of preparing a newly executed oath or declaration and will submit the documents as soon as possible.

Amendments to the Specification

The Office Action states on page 3 that the disclosure is objected to because the Brief Description of Figure 11 does not refer to each of Figure 11A and Figure 11B as present in the Drawings filed on July 21, 2005. Applicants have corrected this error. This amendment adds no new matter, because the addition of the description is a re-statement of the titles of the drawings as filed. This amendment renders this objection moot, and Applicants respectfully request that it be withdrawn.

The Office Action further states on page 3 that an updated priority statement of the instant application's parent provisional and nonprovisional applications should be included. Applicants have included this updated priority statement in the amendments to the specification submitted with this response. As such, this objection is now moot, and Applicants respectfully request that it be withdrawn.

The Office Action also objects to the specification for referring incorrectly to SEQ ID NOs as amino acid or DNA sequences. Applicants have made these corrections in the amendments to the specification submitted with this response, and as such this objection is now moot. Applicants respectfully request that it be withdrawn.

All amendments made to the specification are corrections to errors in identification of certain elements of the disclosure, and as such introduce no new matter to the specification. Applicants respectfully request entry of these amendments to the specification.

Claim Objections

Claim 3 is objected to because the word "Lysine" should not be capitalized, as it is not a proper name. Claim 3 has been canceled, thus rendering this objection moot.

Claim 6 is objected to for reciting "...wherein the modified arrestin further comprises a label..." The Office Action states that the specification provides a limiting definition of the term "modified arrestin" on page 20 of the specification: ""Modified arrestin" means an arrestin that has one or more ubiquitin molecules moieties and a label molecule associated or attached to the arrestin". Applicants respectfully submit that the instant claims as amended recite an "arrestin chimera" rather than "modified arrestin". The term "arrestin chimera" does not encompass a protein with a label molecule associated or attached to the arrestin. As such, this objection is moot.

Applicants respectfully request withdrawal of the objections to the claims.

Claim Rejection under 35 USC §101

Claims 1-6 and 18-22 are rejected under 35 U.S.C. §101 because the claimed invention allegedly is directed to non-statutory subject matter. Applicants respectfully disagree.

Applicants respectfully submit that as amended, the present claims recite an "arrestin chimera". Such a chimera is not a "naturally occurring product" that would be considered non-statutory subject matter.

As such, the currently pending claims meet the requirements for patentable subject matter under 35 U.S.C. §101. Applicants respectfully request that this rejection be withdrawn.

Claim Rejection under 35 USC §112, second paragraph

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants submit that as amended, Claim 7 clarifies that the arrestin chimera comprises the amino acid sequence of SEQ ID NO: 2, 4, or 6. As such, the requirements of 35 U.S.C. §112 are fulfilled, and Applicants respectfully request that this rejection be withdrawn.

Claim Rejection under 35 USC §112, first paragraph, enablement

Claims 1-7 and 18-22 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to enable a person skilled in the art to make and use the invention commensurate in scope with the claims. In view of the amendments to the claims and the remarks made herein, this rejection is respectfully traversed.

As will be appreciated, the test of enablement is whether one reasonably skilled in the art could make or use the invention as claimed from the disclosure in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989). *See* also MPEP §2164.01. One way to determine if undue experimentation is required is to utilize the *Wands* factors: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." All of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).

The Office Action states on page 7 that claim 1 encompasses a vast genus of modified arrestin comprising various configurations of variants of arrestin or ubiquitin, each of which must be constructed and tested to see if they meet the recited functional limitations. Applicants respectfully submit that "modified arrestin" does not encompass such a "vast genus" of proteins that one of skill in the art would be required to undertake an undue level of experimentation to determine if a particular configuration of arrestin and ubiquitin is encompassed by the claimed invention. However, solely to expedite prosecution and without conceding to the propriety of this rejection, Applicants have amended the claims to recite "arrestin chimera" rather than "modified arrestin". Applicants submit that an "arrestin chimera" according to the present claims is sufficiently enabled by the present specification. Arrestin chimeras are described throughout the

specification, and multiple working examples describe assays utilizing such chimeras, as the Office Action itself notes on page 6. As such, an arrestin chimera according to the present claims fulfills the requirements for enablement under 35 U.S.C. §112 first paragraph.

Applicants further submit that although some experimentation may be needed to determine whether a particular configuration of arrestin and ubiquitin displays the functional elements recited in claim 1 (such as increased affinity for GPCR such that the chimera remains associated with the GPCR and traffics with the GPCR into endosomes, and does not dissociate from the GPCR at or near the plasma membrane) the amount of experimentation that might be so required would not rise to the level of "undue experimentation". Unpredictability of whether a particular configuration of arrestin and ubiquitin displays the functional elements recited in claim 1 is balanced by the ease and routine nature of assays to detect those functional elements. The present specification provides multiple working examples of such assays (see for example pages 51 through 60). The present specification also cites multiple references that further describe protocols and assays known in the art that could be used to determine whether a particular arrestin chimera falls within the scope of the present claims.

The Office Action repeatedly states that variants encompassed by the claims would "need to be tested prior to using the full scope of the claims." Applicants respectfully submit that practitioners in the chemical and molecular biology arts frequently engage in extensive modification of reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue. *see Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986). Thus, in contrast to the assertion in the Office Action that the specification does not enable the constructs represented by SEQ ID NOs. 4 and 6, Applicants submit that the specification provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation, because the assays described in the Examples section of the present specification as well as assays known in the art would be available to one of skill in the art to determine whether a particular chimera is encompassed by the present claims. Accordingly, the specification clearly enables the subject invention as demonstrated in view of the relevant *Wands* factors.

Furthermore, the Applicants note that the presence or absence of working examples is but one factor to be taken into consideration in determining whether the specification is enabling for the full scope of the claims. Under MPEP § 2164.02 the consideration is whether one skilled in the art would be expected to be able to extrapolate the provided examples across the entire scope of the claim. One of skill in the art would be able to use the description of the arrestin chimeras and their functional elements provided in the present specification to practice the claimed invention. Applicants submit that it would be reasonable to conclude

that one skilled in the art would be able to extrapolate the working examples provided in the specification across the across the entire scope of the claims without excessive and undue experimentation using methods described in the present specification and known in the art.

In sum, the amount of experimentation required to subject invention would not be undue and excessive because working examples have been provided, guidance is given on how to practice the claimed invention, and one of skill in the art would be able to perform the experiments as a matter of routine. The specification therefore provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation. Accordingly, the specification clearly enables the subject invention as demonstrated in view of the relevant *Wands* factors. Applicants respectfully request that this rejection be withdrawn.

Claim Rejection under 35 USC §102

Claims 1-6 and 18-22 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Shenoy *et al*, 2001. Science. 294: 1307-1313 ("Shenoy"). Applicants respectfully disagree.

To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is either expressly found or is inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. *See MPEP § 2131*. Applicants submit that each element of the claims now pending have not been identified in the art presently of record, and that rejection under §102(b) is therefore improper.

The present claims recite an "arrestin chimera" that has an increased affinity for a GPCR, as compared to the affinity of a wild-type arrestin for a GPCR, wherein increased affinity means that the arrestin chimera remains associated with the GPCR and traffics with the GPCR into endosomes, and wherein the arrestin chimera does not dissociate from the GPCR at or near the plasma membrane. Shenoy neither discloses nor suggests an arrestin chimera according to the claimed invention. The β-arrestin2 described in Shenoy is a wildtype arrestin that has not been altered aside from being cloned into an expression vector (see note 26 on page 1313). There is no disclosure of a modified arrestin or arrestin chimera in Shenoy that shows an increased affinity for GPCR over a wild-type arrestin. Shenoy does not describe an arrestin chimera comprising an arrestin or a fragment of arrestin and a ubiquitin moiety or a fragment of ubiquitin. As such, Shenoy does not describe every element of the present claims and cannot therefore support a rejection under 35 U.S.C. §102(b). Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1266 (direct line).

Respectfully submitted,

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Dated: July 28, 2008 By: _____
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